Dkt. 55424-A-PCT-US/JPW/GJC

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Anne Marie Schmidt and David Stern
U.S. Serial No.	:	Not Yet Known (Continuation Application of PCT/US99/08427, filed 16 April 1999)
Filed	:	Herewith
For	:	A METHOD FOR INHIBITING TUMOR INVASION OR SPREADING IN A SUBJECT

1185 Avenue Of The Americas
New York, New York 10036
October 12, 2000

Assistant Commissioner for Patents
Washington, D.C. 20231
Box: Patent Application

Sir:

PRELIMINARY AMENDMENT TO THE ACCOMPANYING CONTINUATION APPLICATION FILED UNDER 37 C.F.R. §1.53

Applicants request that the following amendment be made in the above-identified application:

In the Specification:

On page 1, after the title and before line 5, please delete the paragraph and insert the following new sentence:

> --This application is a continuation of PCT International Application No. PCT/US99/08427, filed 16 April 1999, designating the United States of America, which is claiming the priority of U.S. Serial No. 09/062,365, filed April 17, 1998, the contents of which are hereby incorporated by reference into the present application.--

In the Claims:

Please cancel claims 1-41 without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in a future continuation or divisional application.

Please add new claims 42-81 as follows:

--42. (New) A method for inhibiting tumor invasion or metastasis in a subject which comprises administering to the subject a therapeutically effective amount of a soluble Receptor for Advanced Glycation Endproducts (RAGE)--

--43. (New) The method of claim 42, wherein the soluble RAGE comprises a polypeptide having a sequence identical to the sequence of human RAGE (SEQ ID NO:1) beginning from alanine at position 1 and ending at serine at position 332 of human RAGE.--

--44. (New) The method of claim 42, wherein the soluble RAGE comprises a polypeptide having a sequence identical to the leader sequence of human RAGE (SEQ ID NO:2) beginning at methionine at position 1 to glycine at position 22 linked to the alanine at position 1 of SEQ ID NO:1 and ending at isoleucine at position 98 of SEQ ID NO:1.--

--45. (New) The method of claim 42, wherein the administration is effected by introducing into the subject a replicable vector containing a nucleic acid encoding the soluble RAGE.--

--46. (New) The method of claim 42, wherein the tumor is a neuronal tumor.--

--47. (New) The method of claim 45, wherein the replicable vector is a plasmid, an attenuated virus, a phage, a phagemid or a linear nucleic acid.--

--48. (New) The method of claim 42, wherein a pharmaceutically acceptable carrier is administered to the subject during the administration of the soluble RAGE.--

--49. (New) The method of claim 42, wherein the administration is via intralesional, intraperitoneal, intramuscular or intravenous injection; infusion; intrathecal administration; subcutaneous administration; liposome-mediated delivery; or topical, nasal, oral, ocular or otic delivery.--

--50. (New) The method of claim 42, wherein the soluble RAGE consists essentially of a polypeptide having an amino acid sequence identical to a V domain of a naturally occuring soluble RAGE.--

--51. (New) The method of claim 42, wherein the soluble RAGE consists essentially of a polypeptide having an amino acid identical to a C domain of a naturally occurring soluble RAGE.--

--52. (New) The method of claim 42, wherein the subject is a mammal.--

--53. (New) The method of claim 52, wherein the mammal is a

human.--

--54. (New) The method of claim 42, wherein the soluble RAGE is administered daily, weekly or monthly.--

--55. (New) The method of claim 42, wherein the therapeutically effective amount comprises a dose from about 0.000001 mg/kg body weight to about 100 mg/kg body weight.--

--56. (New) The method of claim 42, wherein the therapeutically effective amount comprises a dose of from about 100 ng/day/kg body weight to about 200 mg/day/kg body weight.--

--57. (New) A method for identifying an agent which inhibits tumor invasion in a local cellular environment which comprises:

(a) providing a solid support coated with amphoterin;

(b) contacting the solid support with a tumor cell which expresses receptor for advanced glycation endproducts (RAGE) under appropriate cell culture conditions for cell migration and growth;

(c) admixing to the tumor cell culture of step (b) an agent to be tested;

(d) determining the amount of spreading of the tumor cells on the solid support, and

(e) comparing the amount of spreading of the tumor cells

determined in step (d) with the amount of spreading determined in an identical tumor cell culture in the absence of the agent, wherein a decrease in the amount of spreading determined in step (d) indicates that the agent is identified as an agent which inhibits tumor invasion in the local cellular environment.--

--58. (New) The method of claim 57, wherein the tumor cell is a eukaryotic cell.--

--59. (New) The method of claim 57, wherein the tumor cell is a cell taken from a subject.--

--60. (New) The method of claim 59, wherein the subject is a human, a mouse, a rat, a dog or a non-human primate.--

--61. (New) The method of claim 57, wherein the agent comprises a peptide, a peptidomimetic, a nucleic acid, a synthetic organic molecule, an inorganic molecule, a carbohydrate, a lipid, an antibody or fragment thereof, or a small molecule.--

--62. (New) The method of claim 61, wherein the antibody is a monoclonal antibody.--

--63. (New) The method of claim 61, wherein the antibody is a polyclonal antibody.--

--64. (New) The method of claim 61, wherein the fragment of the antibody comprises a Fab fragment.--

--65. (New) The method of claim 61, wherein the fragment of

the antibody comprises a complementarity determining region or a variable region.--

--66. (New) The method of claim 61, wherein the peptide is a synthetic peptide or a peptide analog.--

--67. (New) The method of claim 61, wherein the peptide comprises at least a portion of the sequence -Asp-Ala-Glu-Phe-Arg-His-Asp-Ser-Gly-Tyr-Glu-Val-His-His-Gln-Lys-Leu-Val-Phe-Phe-Ala-Glu-Asp-Val-Gly-Ser-Asn-Lys-Gly-Ala-Ile-Ile-Gly-Leu-Met-Val-Gly-Gly-Val-Val- (Seq. I.D. No. 3).--

--68. (New) The method of claim 61, wherein the peptide comprises at least a portion of the sequence -Gly-Ser-Asn-Lys-Gly-Ala-Ile-Ile-Gly-Leu-Met- (Seq. I.D. No. 4).--

--69. (New) The method of claim 61, wherein the peptide has the amino acid sequence A-Q-N-I-T-A-R-I-G-E-P-L-V-L-K-C-K-G-A-P-K-K-P-P-Q-R-L-E-W-K (Seq. I.D. No. 5).--

--70. (New) The method of claim 61, wherein the peptide has the amino acid sequence A-Q-N-I-T-A-R-I-G-E (Seq. I.D. No. 6).--

--71. (New) The method of claim 61, wherein the agent is a soluble human RAGE.--

--72. (New) The method of claim 61, wherein the agent is an extracellular portion of human RAGE.--

--73. (New) The method of claim 61, wherein the agent

inhibits an interaction between the tumor cell and an extracellular matrix molecule.--

--74. (New) The method of claim 61, wherein the extracellular matrix molecule is a laminin, a fibronectin, amphoterin, a cadherin, an integrin or a hyaluronic acid.--

--75. (New) The method of claim 74, wherein the integrin is an αVβV integrin, an αVβIII integrin, or an αIβII integrin.--

--76. (New) The method of claim 61, wherein the agent inhibits binding of RAGE to amphoterin.--

--77. (New) The method of claim 61, wherein the agent binds to RAGE.--

--78. (New) The method of claim 61, wherein the agent binds to amphoterin.--

--79. (New) A pharmaceutical composition which comprises a therapeutically effective amount of the agent identified in claim 57 and a pharmaceutically acceptable carrier.--

--80. (New) The pharmaceutical composition of claim 79, wherein the carrier is a diluent, an aerosol, a topical carrier, an aqueous solution, a replicable nucleic acid vector, a liposome, a magnetic bead, a nonaqueous solution or a solid carrier.--

--81. (New) A method for inhibiting tumor invasion or

metastasis in a subject which comprises administering to the subject a therapeutically effective amount of the pharmaceutical composition of claim 79.

REMARKS

This application is a continuation of PCT International Application No. PCT/US99/08427, filed 16 April 1999, designating the United States of America and claiming priority of U.S. Serial No. 09/062,365, filed April 17, 1998. Accordingly, the parent application, PCT International Application No. PCT/US99/08427, is pending today in the United States of America pursuant to 35 U.S.C. §363, and the subject continuation application is co-pending therewith in fulfillment of the provisions of 35 U.S.C. §120.

By this Preliminary Amendment, applicants have hereinabove amended the specification on page 1 to insert the continuation data. Applicants maintain that the amendments to the specification present no issue of new matter and are fully supported by the specification. Applicants have amended the specification to recite the continuing data for the above-identified application.

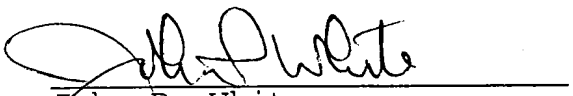
Claims 1-41 were pending in the subject application. By this Amendment applicants have canceled claims 1-41 without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in a future continuation or divisional application. Applicants have hereinabove added new claims 42-81. Support for these new claims may be found in original claims 1-41 and inter alia in the specification, for example, on page 38, line 19 - page 41, line 30; pages 9-17. New claims 42-81 raise no issue of new matter. Accordingly, upon entry of this

Amendment, claims 42-81 will be pending and under examination.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee other than the filing fee of $535.00 is deemed necessary in connection with this Preliminary Amendment. However, if any other fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Reg. No. 28,678
Attorney for Applicant
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400